

**a**

TALE-3X Flag ChIP-seq Peaks

chr location	Rep1 tags	Rep2 tags	pvalue
chr1:47,646,591-47,647,590	25	20	0.01
chr1:17,221,975-17,222,974	3	8	0.14
chr5:78,850,956-78,851,955	5	1	0.21
chr17:51,183,234-51,184,233	2	4	0.15

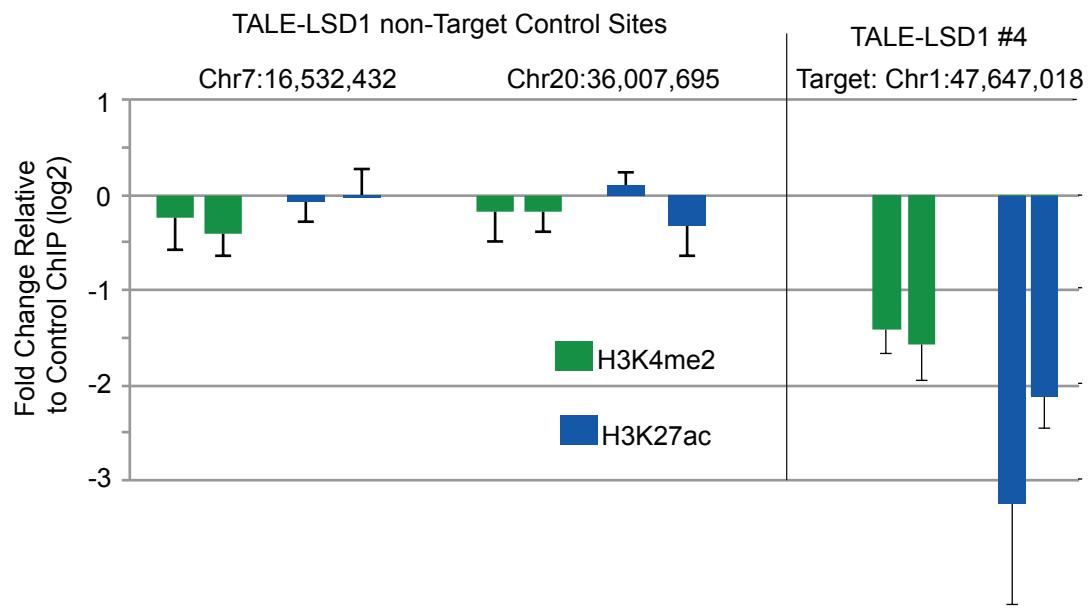
**b**

Target Sequence	TALE-3X Flag ChIP tags per 1kb bin	Input tags per 1 kb bin
18/18 Target (n=1)	17.5	1
17/18 Targets (n=2)	0.5	0.5
16/18 Targets (n=52)	0.40	0.58

**Supplementary Figure 1. Specificity of TALE binding determined by TALE-3X Flag ChIP-seq.**

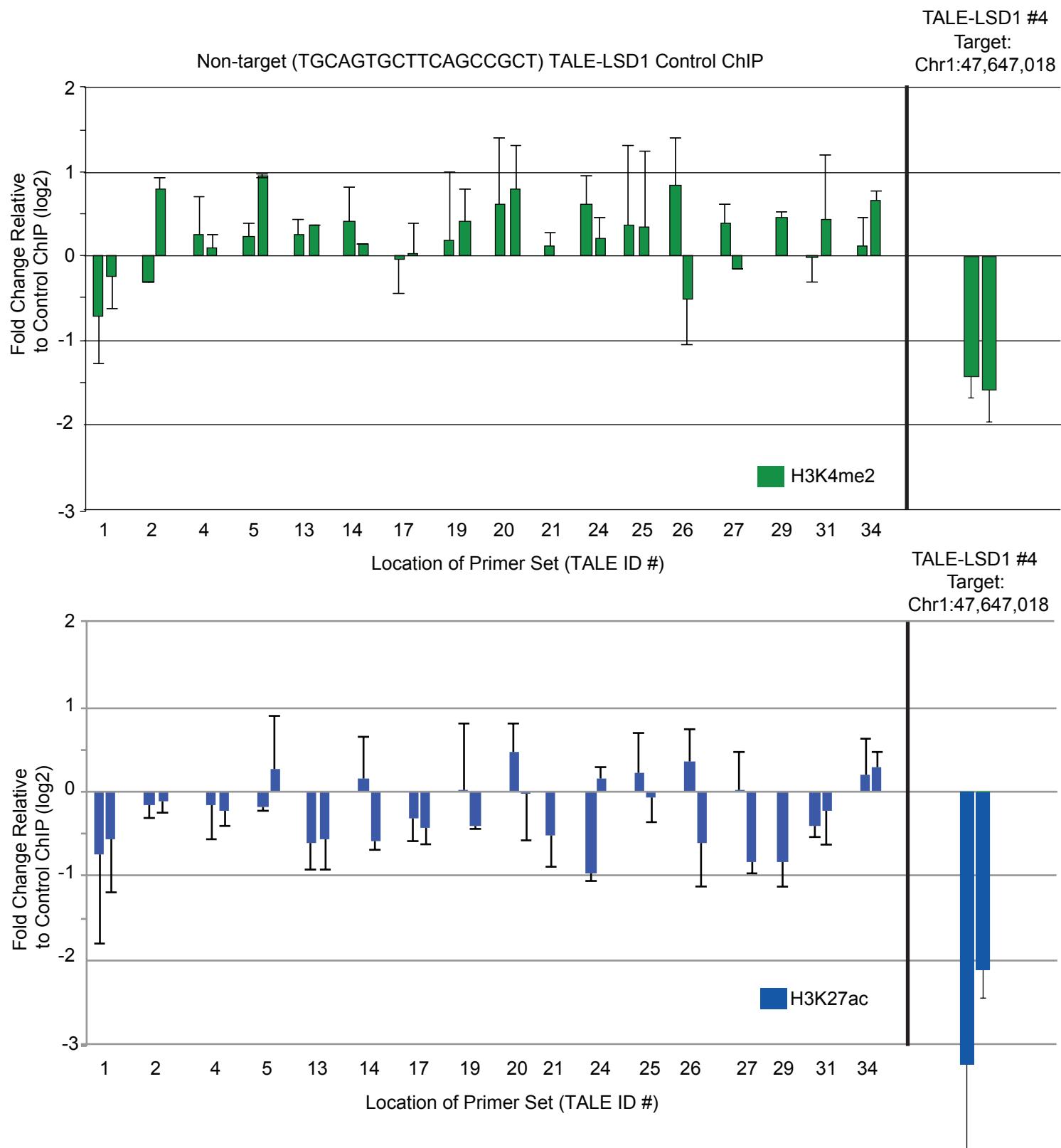
(a) Peak calls using MACS in two biologically independent replicates along with reads falling within a 1 kb window around the peak. Yellow shade indicates the target locus. P-values calculated by comparison of both biological replicates to the input control library.

(b) The sequence read count at 54 genomic loci with 1 or 2 mismatches compared to the perfect match target locus for the TALE-3X Flag.



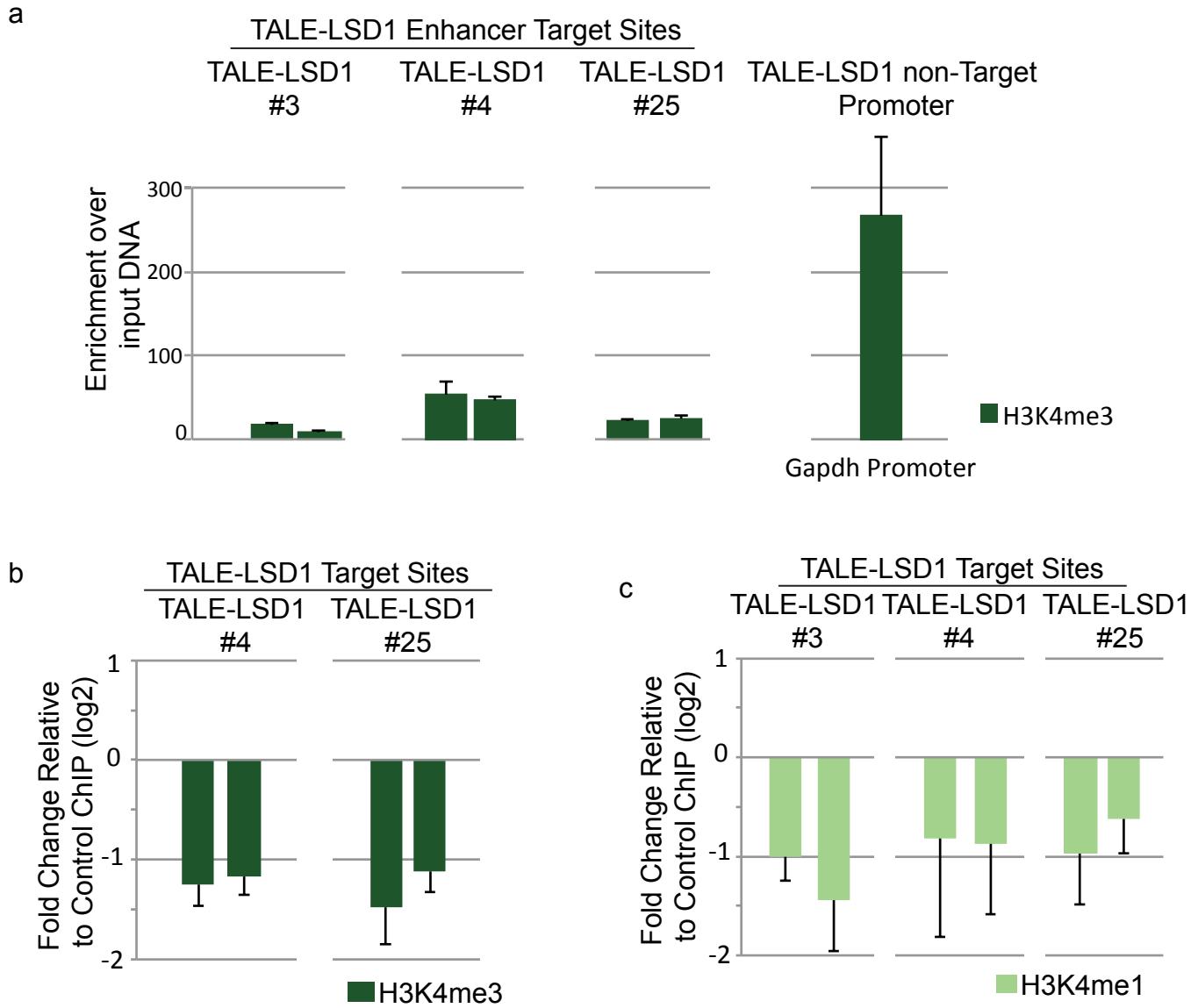
**Supplementary Figure 2. ChIP-qPCR to test for off target effects of TALE-LSD1.**

ChIP-qPCR for H3K4me2 (green) and H3K27ac (blue) at two non-target control enhancers. For comparison, the data from the target enhancer is shown.



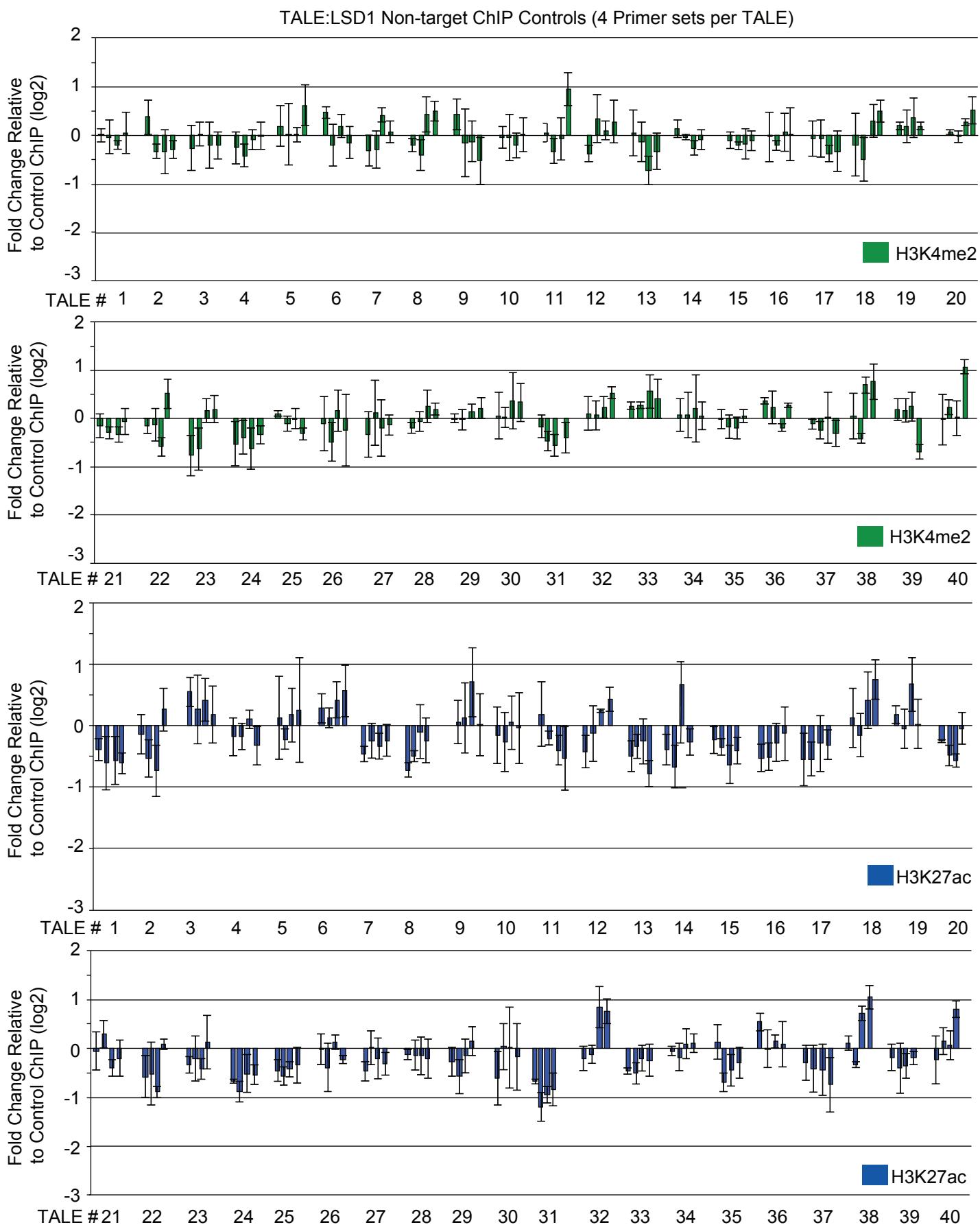
**Supplementary Figure 3. ChIP-qPCR values for the non-target control TALE-LSD1.**

A TALE-LSD1 construct targeting a sequence not present in the human genome was transfected into K562 cells as a control for non-specific effects. Data is shown as ratio of enrichment to mCherry plasmid control for a subset of enhancers shown in figure 2. For comparison, an 'on target' TALE-LSD1 construct at it's targeted enhancer is shown (TALE-LSD1 #4).



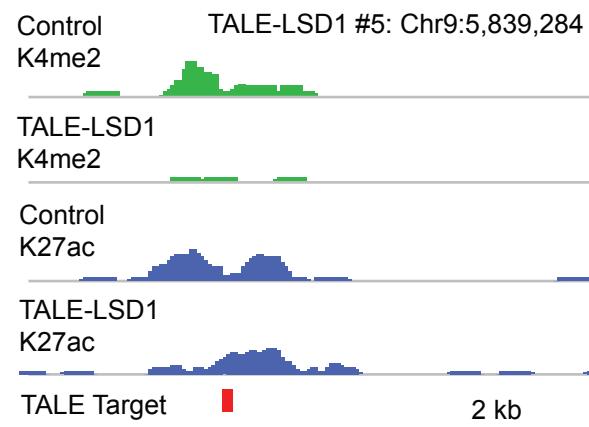
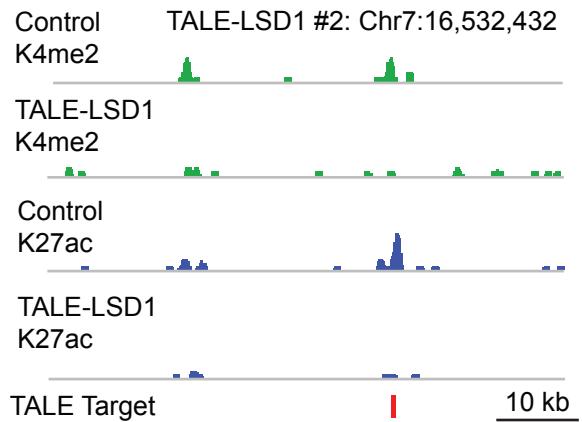
#### Supplementary Figure 4. ChIP-qPCR to test for effects of TALE-LSD1.

- (a) ChIP-qPCR enrichment of H3K4me3 for three target enhancers, selected based on prior evidence of H4K4me3 (#4, #25) and one typical enhancer (#3) lacking K4me3. For comparison, data from a H3K4me3 enriched promoter is shown.
- (b) ChIP-qPCR for H3K4me3 (dark green) at the two TALE-LSD1 targeted enhancers that showed some H3K4me3 enrichment. The data represent the decrease in enrichment at the target enhancer.
- (c) ChIP-qPCR enrichment of H3K4me1 for target enhancers of three TALE-LSD1 fusions. The data represent the decrease in enrichment at the target enhancer.

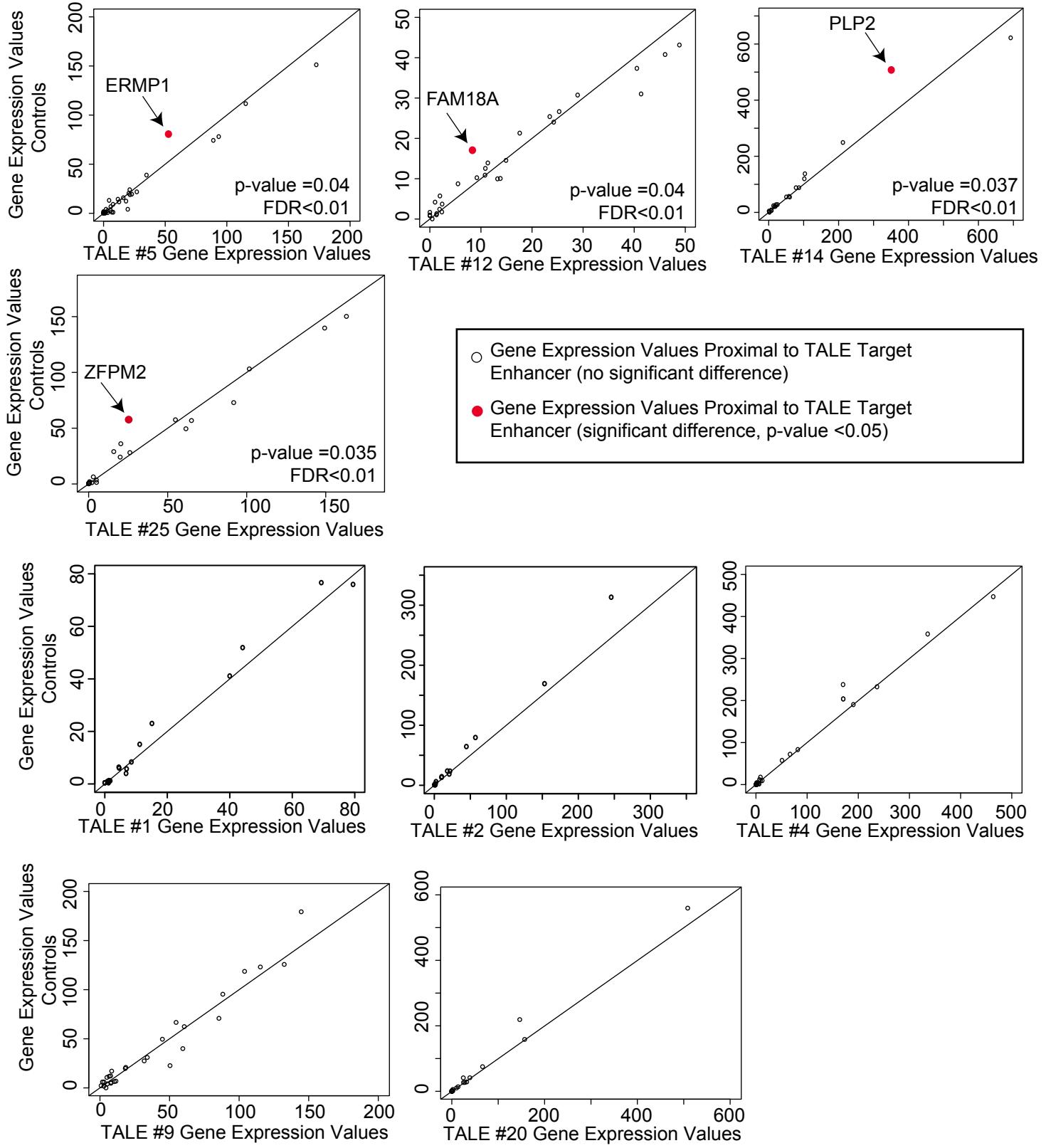


**Supplementary Figure 5. ChIP-qPCR for H3K4me2 and H3K27ac at non-target sites.** Data is shown for all 40 TALE-LSD1 constructs used in Figure 2. Four primer sets were used to measure ChIP enrichment at two non-target enhancer loci for each TALE construct. No non-target enhancer showed a significant decrease (>2 fold decrease in 2/4 primer sets) in ChIP enrichment.

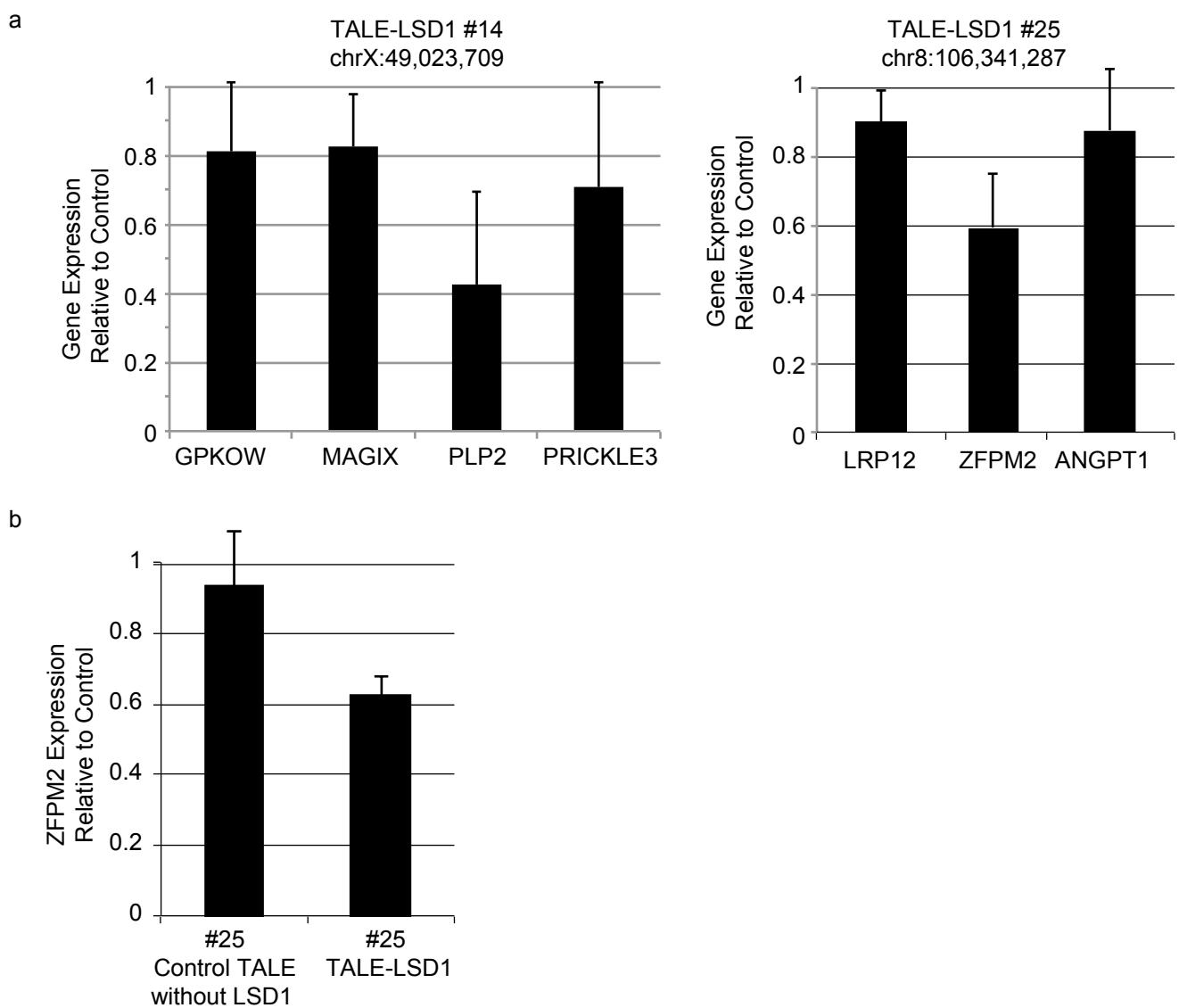
H3K4me2 and H3K27ac ChIP-seq of  
TALE-LSD1 transfected Cells



**Supplementary Figure 6.** ChIP-seq maps for H3K4me2 and H3K27ac for control cells and cells transfected independently with 2 TALE-LSD1 fusions.



**Supplementary Figure 7. Mean normalized 3' Digital Gene Expression Values for the 10-25 genes nearest the TALE target enhancer.** Genes with values below 10 were considered unexpressed in K562 cells. Red data points represent genes with a significant decrease in the TALE-LSD1 transfected cells. Significant decrease was considered if both biological replicates represented the two outlying values across all 22 RNA-seq datasets (see Methods).



**Supplementary Figure 8. Quantitative PCR confirmation of 3' DGE.** (a) RT-qPCR expression analysis for genes near two TALE-LSD1 target sites.

(b) RT-qPCR data showing gene expression for Zfpm2 in cells transfected with a TALE #25 control plasmid that lacks the LSD1 protein, with data from the TALE-LSD1 for comparision. Error bars represent +SEM, n=2 biological replicates.

**Supplementary Table 1. TALE Array Target Sequences**

TALE ID#	chr #	TALE Target Sequence
1	chr12:25,845,475	TTCAGTTGTGGTATCTG
2	chr7:16,532,432	TACCATGTCTTCTAAG
3	chr3:141,765,325	TTTACAGAGCTGTGGTCACT
4	chr1:47,647,018	TCCGTGGCTGCCAGTCTG
5	chr9:5,839,284	TGCATATACTTTTAATG
6	chr1:47,646,996	TCCAGGAGCGCGCCTGAG
7	chr7:129,598,655	TGCCTGTGAGGAACAGCTGT
8	chr2:169,708,409	TGCAGACATCTCCAGGCTCT
9	chr9:102,832,599	TAATTGTACATGGTTACAT
10	chr15:38,894,009	TGTTAGTTACCATATTGTGG
11	chr8:106,347,824	TCCAGTCCCTGGCTCCCATG
12	chr16:10,832,743	TGGCTAATTTTGGTATTTT
13	chr4:145,245,496	TGGCTTCCTCCCTTTG
14	chrX:49,023,709	TAGCCGCGAGGAAGGCG
15	chr5:162,806,718	TAAAGACCTGTTACCCAATT
16	chr4:145,050,452	TCGTTTTCTTTTGGAAG
17	chr7:129,515,859	TTCTAAATTGAGGTGCTG
18	chr10:11,183,638	TCAATCATTGCATGTTATT
19	chr17:8,323,819	TTGCATCTGGGACAGATG
20	chr11:5,245,852	TTGATGGTAACACTATG
21	chr1:182,269,308	TTATCTCCCTCACCCAG
22	chr1:198,568,183	TGGTTAGAAACACAGCTGCC
23	chr6:138,240,975	TTCATGGTTCAATAAGACT
24	chr3:150,169,053	TACATAAAATTTAAGG
25	chr8:106,341,287	TTAAGCTTCTGAAGTCAG
26	chrX:119,619,445	TGATCTTCATTTTAAAG
27	chr21:15,825,632	TGGTATGAGTTGAAAATG

28	chr8:106,376,850	TAAGTCTACATATAGTATCC
29	chr11:16,617,852	TAAAATGCACTCACAATG
30	chr19:14,496,304	TCTCTGAATCCCCTGGTGAC
31	chr6:119,634,206	TTAACACAGATAAGGGAG
32	chr1:47,646,977	TGGTGCCTTATCAGCCTT
33	chr8:106,256,324	TCAATACCCCACAAAGAAGC
34	chr20:36,007,695	TCTCTACCTTGGAGGCTG
35	chr1:166,674,281	TAGAAAATACAACCTCAG
36	chr11:48,082,936	TCCTGGAAAAGCCCTCTATG
37	chr14:23,030,549	TAAGTTGCAAACAAGCTCC
38	chr19:23,907,083	TGGCTTCCTAGGCAGAAGT
39	chr10:80,948,325	TCACGCCCTTGCGGCCAGAG
40	chr18:32,630,094	TCACTGTGTACCTTTTATG
non-Target	N/A	TGCAGTGCTTCAGCCGCT

**Supplementary Table 1**      **Primer Sequences Used**

TALE ID #	ChIP qPCR Primer Set	F	R
1		1.1 GGAATCGTGAATACCCCTGA	AACATGCAGGTCTGCTTCC
1		1.2 GGAATTGGCCTGCAGAATT	GTACACCATTGGCTGGCTCT
2		2.1 TACTGACCCATGAGCACAGC	CCCCACTGCCATCCTACTTA
2		2.2 GAGTGTGAGCAATGAGCA	TGTGCGTATGCATTTGTTCT
3		3.1 AGCACACAATTGCTCATCA	ACGTGCACATGGAACAAGAC
3		3.2 CTGCCAAGTTCTGGTTGGT	GAGACAAAATAGCGGGGACA
4		4.1 AAGAGGACATTCTGGCTGA	CCTGCCTCCTAACGCTTCCTT
4		4.2 GACCTGACTCGAACCCACTC	GCCTCTGCTAACGGCACAAAC
5		5.1 TGCCTAGGAAGGCACTTGTC	GGCTGGAGATCAGCTTTTG
5		5.1 TGTCTGGAACGGTTCACT	TTTCTCCTTGGGCATCTG
6		6.1 AAGAGGACATTCTGGCTGA	CCTGCCTCCTAACGCTTCCTT
6		6.2 GACCTGACTCGAACCCACTC	GCCTCTGCTAACGGCACAAAC
7		7.1 CCCTTGACCAGGTAGGTTCA	AAGGAGGGCTCCAGTTCAT
7		7.2 TGGTCCAATGAGTAGCAGAGC	GGGGATTTCACACTGGTG
8		8.1 TGTCTGCACAAATTGCTGTG	CTTGGGAGGGTTAGAGAC
8		8.2 ACTCAAAGGTGGGTGTGAGG	TCCGATAATCTGGTCCAAGG
9		9.1 CCCAGGAAACTTGATGAGAGA	TGTGGAAGGAGTGAGTGAACA
9		9.2 GGGTTTCATGAAGCTTGAA	TTTCGTATTGCATCCCATCA
10		10.1 GCTGAGCTTTCAGGTAGGC	GCTCCAAAAAGATGCAAGT
10		10.2 GGGCCCTCCTATACTTGGA	TGGACTGGAGGAACATAGC
11		11.1 TGCTACGTGCAGCGTATTCT	TGCAACGCTATTCTCAGGA
11		11.2 AGCATTTCAGCCTCAGTGG	CCTTGTAGCACCTCTGTCCA
12		12.1 CAGACTTCTGGAACGCAGTG	TGTGACAGGCCAAGTCTCAG
12		12.2 CTGACGGTTATGAGCAGCA	GTTTCCCACAGTCCCTGAA
13		13.1 TGAAGTCCACATGTTAGCTCCT	TGGAAGGAATGTGATTCCACT
13		13.2 TTCAACAGCAACCAGGAATG	AAGCTAAAAAGAAAAACTCAACA
14		14.1 CCATTTCCGTACATGGTGA	CTGGCTGTAGGGCTCTGTTC
14		14.2 GACGGGGAAGGAAGAAAGAA	TCCCAGCTCGCAGCTT
15		15.1 TACACAAACAGCACCCACACA	CCCCATTTCAGTTCTTCTCA

15 15.2 TCTTCTGGGTTGTTGGCTA  
16 16.1 TCCAAC TCAATGCCTTTCTG  
16 16.2 AATGGCTCTGGAGAAAAGCA  
17 17.1 TGTGAACCTCGAGAAGTGTGA  
17 17.2 GTCATGTCCAGCAGGATGC  
18 18.1 ACGATGGAGGACATTGGAAG  
18 18.2 CTGCAAACAAGGTCTTGGAC  
19 19.1 GTGACCTTGGAGACGTTGCT  
19 19.2 AAGAGAAGGAGAACCAAGCCTTA  
20 20.1 GATTCCGGGTCACTGTGAGT  
21 21.1 GGAAGAAAGGAAGGTAGGAAGG  
21 21.2 GCTGAGACCACCCACTCTTC  
22 22.1 TCACACATCACTGCGTTCA  
22 22.2 AGGGAGCACTCTAGGGATGG  
23 23.1 CCACTAAACCGCAACCAAAG  
23 23.2 CGTTTCTCCCTGGGTTCTT  
24 24.1 CTGCC CCAAAGAAAGGTAT  
24 24.2 TTGACATTAGGTCCAGGTTGA  
25 25.1 TCATTTGGTAGCCTTCTGC  
25 25.2 GATGATTGGCTTTGCGATA  
26 26.1 GACGTGTTGGTGCATACCTG  
26 26.2 TCAAGAGTACGGCAATCACG  
27 27.1 GACCACCGGTCTTCTCATGT  
27 27.2 TAGGGTGTGGATGTGGAACA  
28 28.1 TCCTGTAAAGTCCTCAGATCAACA  
28 28.2 TTGGTCTTGGCCTTCTAGG  
29 29.1 CAGCCTTCTAGGAATCACAAA  
30 30.1 GTGAACCACCAAGCACAGC  
30 30.2 GGCTACAGCGTCTCCTGTG  
31 31.1 TAAGGCCGGTCTATCACAGC  
31 31.2 ACTGCCTGCCTGGAGTCTAC

GGCACCATGTGA ACTCTCCT  
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AGCAGGGGTGGAGAGAAAAT  
CACACACCACACCCACAAC  
GCAGTCTCAGCACCTCAACC  
TCGCTCACTGAGGAATGATG

			TGGGGGTCAGAGAGAGAATG
32	32.1	TACACCGCGAAGGGATAGTC	GCCTCTGGAGTGCAGTACCT
33	33.1	GGGCCCCAGACTTAATTG	CCCCCAAATTCCATTATTCC
33	33.2	CCCAGATATTCCTGCTCCA	ACAATGGGGCTGCCTGAG
34	34.1	GAGGGAGCGAGCCATAGTG	TCGAAAGCTACACGGCTCTT
34	34.2	GGAGGAGGGTGGTCTCTCAT	AAACCCCTATGGGCAACTCT
35	35.1	TGGGTGAGGAAGGAGAAAGA	CAATCATTGCCAACACAGG
36	36.1	CTGGCCCTCTCTCCTTTCT	TCGCACCTGTGTGAGAGGTA
36	36.2	GTCTGAGGAAAGGCACCTGA	GGTGTTGCGGAAAACACTTT
37	37.1	AGCGACAAAAGGTCAACAGA	CAGTCTGGGCAACAGAACAA
37	37.2	CCTAAGAACATCAGAAACGCAATG	CTGTAACCCTACCCCCAACCC
38	38.1	AACGAAACACAACACCTGCACA	TCAGAAGGTGTGGGGAAAAG
38	38.2	CAGAACAAAATGGAGTCTTAGCC	CGTCTGTGCGAAGAGAACG
39	39.1	ATGGCTTCATGAAGCTGGA	TTCCCGGTTAGATGAGTTGG
39	39.2	AAAGCATTTCGCCATCCAG	TGGGAACCTCTCCATCTCAC
40	40.1	GCCCTCCCTTGATAAGAACCC	GGCTAAATGAGGCAGATGCT
40	40.1	CCAAAGTCACATGGATGACAG	
N/A	BC.1	CCTAGGCAACAGTGACACCTATT	AAAAATCAGTTGTGTGTTGTGG
N/A	Gapdh Promoter	GAAGGTGAAGGTGGAGTC	CCCATACGACTGCAAAGACC
TALE ID #	cDNA qPCR Primer Set F		R
#14	GPKOW	CTGAGGGAAAGACATGCTGGA	AGTGAAGCTCCACCACTGA
	MAGIX	CCCAGCTCCACCTGGTTATT	CTAGGGAAGTGCTGCTGCTG
	PLP2	ATGTGTGACCTGCACACCAA	CTTTACCCCTGCGACGATT
	PRICKLE3	GGCACCAAGCACAGAGTTAGC	GACGACCGAAGGCACATATCA
#25	LRP12	GAAGCTCCTCCCTCGTATGG	TCCAAGCTGAGATCGTACCG
	ZFPM2.1	ATCAGATTCCAGCCTGTGC	TGATCACGGAATCAGCAGTG
	ANGPT1	CTGGGACAGCAGGAAAACAG	TAGATTGGAGGGGCCACAAG
	ZFPM2.2	GGCCTGAAAATCTGAGCTGC	CAGTCGTCTGTCTCAACTCCA
	ZFPM2.3	GTACAGCAAAGGGGTCAGC	GAUTGGCAGCTTGTAGCCTT
	ZFPM2.4	GTTTTATCTTTGAAAGGCACAGTC	TTGTGATCACCAAGGTGCAGT
	ZFPM2.5	TCAATTTCAGCTGCTTCCCTCA	CTGGAAATCTGATGGGCACT

SDHA  
TBP

TCTGCACTCTGGGAAGAAG  
TTCCCCATGAACCACAGTTT

CAAGAATGAAGCAAGGGACA  
TGCAATACTGGAGAGGTGGA